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Letters

Functional 3D Printed Patient-Specific Modeling of Severe Aortic Stenosis

Computed tomography (CT) provides high-resolution images of the aortic valve with clear localization of calcium deposition. Three-dimensional (3D) stereolithographic printing can be used to convert these data into a physical model (1,2). We hypothesized that patient-specific, multimaterial, 3D printed models could be created from clinical CT imaging data, and these models would accurately replicate both the anatomic and functional characteristics of severe aortic valve stenosis (AS).

We retrospectively selected imaging data from a pool of patients (N = 250) who had undergone both CT and Doppler echocardiographic studies before transcatheter aortic valve replacement. Electrocardiogram (ECG)-gated mid-systolic CT DICOM (Digital Imaging and Communications in Medicine) images were imported into anatomic modeling software (Mimics X64 15.0, Materialise, Leuven, Belgium) with which the anatomic regions of interest (left ventricular outflow tract [LVOT], aortic valve, and proximal ascending aorta) were isolated and calcified regions identified. By combining the calcified and noncalcified image datasets, we then created 3D fused-material physical models of this patient-specific anatomy. Calcified anatomic regions were printed using a rigid material (VeroWhitePlus RGD835, Stratasys, Rehovot, Israel), and all soft tissue structures (noncalcified cusp segments, LVOT, and ascending aorta) were printed using a rubber-like material (Objet TangoPlus FLX930, Stratasys).

For the functional assessment of these patient-specific AS models, we then coupled each model to our pulsatile flow imaging circuit, which has been previously described (3). In brief, the circuit incorporates a pulsatile pump, arterial compliance/resistance elements, a fill reservoir, and a water bath to facilitate ultrasound imaging. Pressures proximal and distal to the aortic valve construct were measured using high-fidelity pressure catheters (Millar, Houston, Texas). In-line ultrasonic flow transducers (Transonic Systems, Ithaca, New York) assessed transvalvular stroke volume flow. An initial flow condition for the model was chosen to replicate the stroke volume recorded during the clinical echocardiogram. A multifrequency transthoracic transducer and nonimaging probe (iE33, Philips Healthcare, Andover, Massachusetts) were used for functional imaging of the 3D model. Aortic valve area (AVA) (in cm^2) was calculated by the Doppler continuity method such that $AVA_{Doppler}$ = stroke volume/time velocity integral (TVI), where TVI was assessed by continuous wave Doppler across the printed valve construct.

In total, we created 3D printed AS models for 4 different patients and performed functional testing of each model under 7 different flow conditions. Each model demonstrated accurate reproduction of the calcific deposits within the LVOT, aortic cusps, and aortic root. In addition, the shape of the orifice area at the cusp tips was qualitatively very similar in comparison to the corresponding clinical CT. Ultrasound imaging properties of the functional construct were similar in quality to the clinical study. Spectral Doppler evaluation revealed similar signal quality and replication of clinically meaningful hemodynamic values. Mean Doppler AVA was 0.65 ± 0.15 cm^2 (range 0.41 to 0.87 cm^2) and mean Doppler gradient was 36.1 ± 14.7 mm Hg (range 12.6 to 61.3 mm Hg), and correlated well with catheter-derived AVA and mean gradient ($r = 0.975$ and $r = 0.976$, $p < 0.001$, respectively). For each patient model, the $AVA_{Doppler}$ difference between the model and clinical echocardiography study was small (range 0% to 17% difference), with some of that variation being attributable to limitations of the LVOT Doppler method in defining the true LV stroke volume. These data suggest that the geometric valve area of the model was an accurate replication of the patients' valve area, and that the ultrasound properties of the model were sufficient to permit diagnostic quality Doppler imaging (**Figure 1**).

Previous studies have created models of cardiac valves, aortic root, and various congenital structural defects from clinical echocardiographic or CT data (1,4,5). However, these anatomic models were not created to be functional constructs or to permit replication of pathological hemodynamic conditions.

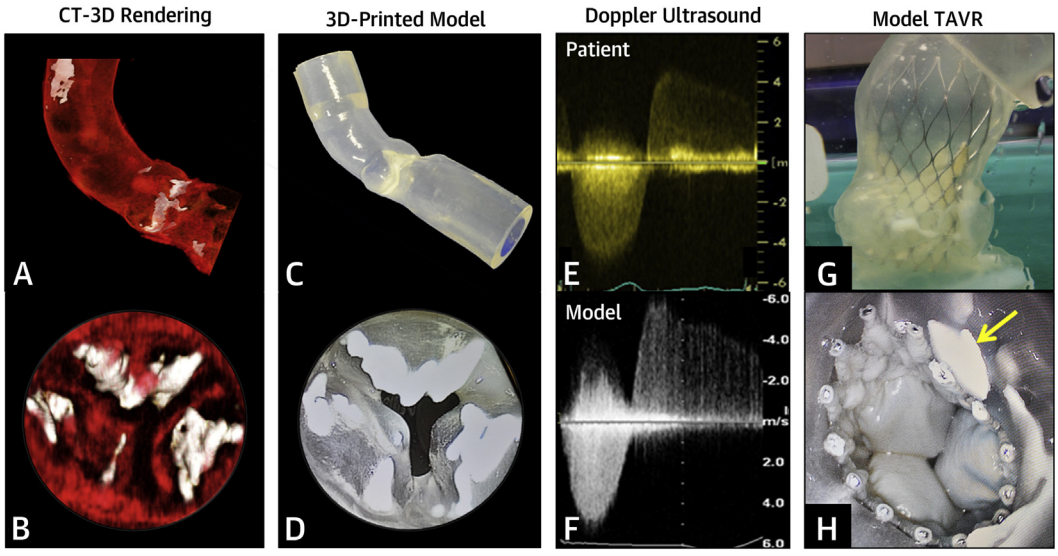

FIGURE 1 CT Data From a Patient With Severe AS

Long-axis **(A)** and short-axis **(B)** views were segmented into soft-tissue structures **(red)** and calcific nodules **(white)**. These DICOM data were manipulated in engineering software to create 3-dimensional (3D) printed fused-material patient-specific models, long-axis **(C)** and short-axis **(D)** views. Functional aortic stenosis was demonstrated with matched Doppler characteristics between the clinical patient study **(E)** and the patient-specific model **(F)**. Deployment of a transcatheter aortic valve within a model is demonstrated **(G)**, with regional "calcific" resistance **(yellow arrow)** to a self-expanding nitinol stent frame as viewed from the left ventricle **(H)**. AS = aortic valve stenosis; CT = computed tomography; TAVR = transcatheter aortic valve replacement.

Severe AS may be an ideal target for 3D printing because the pathological condition is widely acknowledged to be a "fixed" obstruction with relatively immobile valve cusps.

In our preliminary work, we identified that the largest measureable AVA occurred during mid-to-late systole, which was most consistently imaged by CT as the 30% phase of the R-R interval. As such, each model was fabricated from CT imaging data representing only a single moment of the cardiac cycle. Because severe AS is a clinical condition with a relatively fixed AVA, the restricted temporal resolution of CT is potentially only a minor limitation to the modeling objective.

We demonstrated that 3D printed models can replicate both the anatomic and functional properties of severe degenerative AS. These full-scale models of specific patient anatomy and valve function can be created by combining the technologies of high spatial resolution ECG-gated CT, computer-aided design software, and fused dual-material 3D printing. The development of patient-specific models that accurately replicate both anatomic and functional characteristics may have multiple near-future applications.

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Is it Time to Launch *JACC: Early Career*?

We greatly enjoyed reading the recent report by Tong et al. (1). The authors beautifully summarized the current situation of academic cardiology for early-stage cardiologists, presenting current challenges for early career (EC) academic cardiologists, obstacles identified by a survey of current EC members of the American College of Cardiology (ACC), reasons for failure to receive funding from the National Institutes of Health/National Heart, Lung, and Blood Institute, potential solutions, and a call to action with specific recommendations. We respond to this call with a proposal for a dedicated *Journal of the American College of Cardiology* (*JACC*) publication showcasing articles by early career investigators (ECIs). Is it time to launch *JACC: Early Career*?

There are many cardiology fellows, residents, and students interested in pursuing careers in cardiology. The ACC's EC section has approximately 7,000 members. The ACC has taken tremendous initiative to encourage early-stage physicians with the Fellows' Bootcamp, Young Investigator Award at Scientific Sessions, and Fellows in Training and EC Sections with a mentor-mentee database. In an online survey about the ACC's offerings for early-stage cardiologists, 75% of the EC Section rated the ACC's overall value "very strong." Early-stage cardiovascular professionals desire support with research opportunities and academic planning. Eighty-five percent of EC professionals reported seeking an academic position and two-thirds wished to conduct research. Obstacles identified included lack of time, unstable funding, burdensome regulatory compliance, competing against PhDs, overemphasis on relative value unit-based metrics, which can discourage academic pursuits, and insufficient support from institutions. However, is part of the conundrum constituted by lack of dedicated space for publications by ECIs? After all, the final step for successful research is publication.

JACC: Early Career could be launched under the *JACC* flagship in the EC Section, with the current *JACC* editor serving as editor-in-chief. Under his direction, the editor could be the chair of the EC Section/working group chair/ECI with an accomplished research background. ECIs could include students, residents, fellows in training, physician-scientists, and cardiologists within 10 years of completion of fellowship training. For consideration for publication in *JACC: Early Career*, the ECI ought to be the first author. The senior author could be an ECI/designated mentor.

Apart from original articles, unique features could be sections addressing grant writing, ethical considerations, common statistical scenarios, clinical quandaries akin to "Stump the Professor," experiences by seasoned cardiologists with successful careers in research, and success stories by EC cardiologists. This journal would be a resource for the reader to access the latest research by ECIs, learn something clinically relevant, increase knowledge of research methodology, and, most importantly, feel motivated to conduct meaningful successful research. The *JACC* audience would expand to include students and residents and would serve as an opportunity for senior cardiologists to identify ECIs with similar research interests and possibly forge mentee-mentor relationships.

> "We have been fortunate to have great stalwarts in clinical research. Scientists have become the bearers of the torch of discovery in our quest for knowledge."
>
> —Stephen Hawking (2)

JACC: Early Career would enable the next generation to develop the prowess to bear this torch when the time comes.

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REPLY: Is it Time to Launch *JACC: Early Career*?

We thank Drs. Shenoy and Tuliani for their kind letter and novel idea in response to our report (1). We agree that early career academic cardiologists are in need of publications. Publications are the scientific currency that enables early career academic cardiologists to achieve recognition and grants for successful